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Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)	
	09/433,429	KIRKPATRICK, SHAUN A.	
	Examiner	Art Unit	
	Lisa Gransheroff	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *1-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-26,* is/are rejected.

7)☒ Claim(s) *23 and 24* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Pending claims: 1-26.

Election/Restrictions

Applicant's election with traverse of Group II, claims 18-26 in Paper No. 8 is acknowledged. The traversal is on the following grounds, which the Examiner has numbered for purposes of discussion: (i) applicants state that the inventions are "not independent and distinct"; (ii) applicants state that "there is potential limitation of an applicant's financial resources"; (iii) applicants state that 35 USC 121 "does not provide comfort to applicants" against allegations of double patenting in patents issuing on divisional applications; and (iv) applicants state that the classification system is a poor basis for requiring restriction.

This is not found persuasive because of the following. (i) Regarding the phrase "independent and distinct", the MPEP states that the phrase is interpreted as "independent or distinct"; see sections 802 and 803. The inventions of the instant groups are believed by the Examiner to be distinct, and Applicants did not provide arguments to state that they are not distinct. (ii) The MPEP allows for restriction when the Examiner deems it necessary, and Applicants can choose how to proceed with applications in the future and thus determine what their costs are. (iii) It would appear that Applicants are saying that no restriction is proper in view of 35 USC 121 and the cited case law. Clearly this is not reasonable, and it is thus not reasonable to avoid restriction based on this argument. (iv) Regarding the classification of the Groups, as part of the Restriction requirement the Examiner listed the classes and subclasses

because it is standard practice to do so and proper to do so. The justification of the restriction was not on the basis of the classification system, however; rather, the restriction was justified because the inventions of the different Groups are distinct and have recognized divergent subject matter. Further, it would be a serious burden on the Examiner to search, evaluate the search results, and otherwise examine the patentability of the inventions of both Groups.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-17 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

Claim Objections

Claims 23 and 24 are objected to because of the following informalities: The abbreviation "B-UGT" should be written out in its full length in its first appearance in the claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18 and 20 recite a coding sequence for a biological factor or intermediate. It is not clear what is meant by the term "intermediate". The term intermediate could, for example, encompass non-functional molecules, and it is not clear how these would be useful. If claims 18 and 20 are only meant to encompass functional biological factors, then it is not clear why there is a distinction between "biological factor" and "intermediate" in the claim. The metes and bounds of the claims are thus indefinite.

Claim 19 recites the limitation "the vector of claim 8" in the first line of the claim. There is insufficient antecedent basis for this limitation in the claim. For purposes of examination with respect to the prior art, the Examiner will interpret that claim 19 was intended to depend from claim 18.

Claim 20 recites that there is a signal sequence upstream to said coding sequence for a biological factor. This is unclear, since biological factors are often encoded by sequences wherein the coding sequence includes a signal sequence; that is, the coding sequence is for a factor that includes a signal sequence, which may then be cleaved during the process of secretion. The claim is thus unclear, because it could be interpreted as saying that there could be two signal sequences, with the second signal sequence being upstream of the native signal sequence of the biological factor; such a construction might not work, or at the least would have

unnecessarily redundant information. It would be more clear if the claim simply recited that there was a signal sequence downstream from the promoter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 18-20, 25, and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Gorman (EP 0 260 148 A2).

Gorman teaches vectors and Sertoli cells comprising the vectors. The vectors include, for example, "pF8CIS" and "pF8SCIS", which comprises a promoter which is operatively linked to a coding sequence ("cDNA") for a biological factor ("factor VIII") and further comprises a 3' termination sequence ("the SV40 polyadenylation and transcription termination sites"). See pages 9 and 10. The promoter functions in Sertoli cells, as is demonstrated by the Sertoli cells which are disclosed to comprise the vector and which produce factor VIII. See page 11, lines 15-43; page 12, lines 10-46, page 13, and Figs 1 and 2; also see page 7, line 4, which states that TM4 cells are mouse sertoli cells. Since, as noted on pages 13-14 (Example 3), active factor VIII was secreted from TM4 cells, an inherent property of the vector is that there is a signal sequence appropriately located in the vector (downstream of the promoter). Solely to provide

further support for the inherency of a signal sequence in these factor VIII-encoding vectors, the teachings of Wood et al. (U.S. Patent 5,633,150) will be cited here. Wood et al. teach that the coding sequence for factor VIII includes a sequence for a signal peptide upstream of the coding sequence for the mature protein; see Fig. 9 and the description of Figure 9 in column 7, lines 50-62.

Gorman also teaches a vector coding for another biological factor, prorelaxin, and Sertoli cells comprising the vector. The vector comprises a promoter operatively linked to the coding region for the biological factor and a termination sequence. Since the cells produced the biological factor, the promoter functions in Sertoli cells. See pages 17-19.

Gorman also teaches vectors in general that comprise coding sequences for desired biological factors and appropriate sequences for expression or production of the biological factor, and Gorman teaches sertoli cells comprising any of these vectors (see claim 1 and claim 22 on pages 20-21). Note also in the Tables on pages 12, 13, and 19, that the TM4 (sertoli) cells were often better at producing the biological factor than the other cells tested.

Claims 18, 19, and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Jiang et al. (1997. Gene 185:285-290; see also the PubMed printout at the end of the document citing the month of publication as February.).

Jiang et al. teach a vector comprising a promoter which functions in Sertoli cells (from the "SCF" promoter) operatively linked to a coding sequence for a biological factor (luciferase), and Sertoli cells comprising the vector. See page 287, part 2.3, and Fig. 3 on page 288. Since

luciferase activity was measured, the luciferase must have been produced, and thus inherent in the vector is a 3' termination sequence to allow for proper termination.

Claims 18, 19, and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Blanchard et al. (1997. Biology of Reproduction 56:495-500, on Applicant's IDS).

Blanchard et al. teach a vector comprising a promoter (from the Rous sarcoma virus) operatively linked to a coding sequence for a biological factor (lacZ), and Sertoli cells comprising the vector (see page 296, first three full paragraphs in the left column, and the first paragraph of the Results section in the right column). Since lacZ activity was seen, the lacZ must have been produced, and thus the promoter is functional in Sertoli cells, and an inherent property of the vectors is that there is a 3' termination sequence to allow for proper termination.

Claims 18-20, 25, and 26 are rejected under 35 U.S.C. 102(a) as being anticipated by Eskola et al. (April 1998. Molecular and Cellular Endocrinology 139:143-152).

Eskola et al. teach a vector comprising a promoter which functions in Sertoli cells (the SV40 enhancer/promoter) operatively linked to a coding sequence for a biological factor (follicle-stimulating hormone receptor, or FSHR), and Sertoli cells (called MSC-1) comprising the vector. See title, Abstract, and page 144, section 2.3. Since the Sertoli cells expressed the FSHR (see for example section 2.3 and the first paragraph of the Discussion section), an inherent property of the vector is that there is a 3' termination sequence to allow for proper termination. Additionally, since Eskola also teaches that FSH acts via receptors present on plasma membrane of SC (Sertoli cells; page 143, right column), and since the Sertoli cells comprising the FSHR

vector were responsive to FSH, absent evidence to the contrary there is a signal sequence in the vector to allow for secretion of FSHR to the plasma membrane.

Claims 18-20, 25, and 26 are rejected under 35 U.S.C. 102(a) as being anticipated by Ducray et al. (May/June 1998. Steroids 63:285-287).

Ducray et al. teach a vector comprising a coding sequence for a biological factor (ABP) and Sertoli cells comprising the vector. The Sertoli cells (TM4 cells) express the ABP cDNA and secrete ABP (see abstract and page 287, left column). Thus, the vector must have the inherent properties of a promoter functional in Sertoli cells and operatively linked to the coding sequence for ABP and 3' termination sequence for proper termination. Additionally, absent evidence to the contrary, since the ABP is secreted, there must be a signal sequence to direct the secretion.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 18-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gorman, as applied to claims 18-20, 25, and 26 above, and further in view of Builder et al. (U.S. Patent 5,663,304), Meulien (U.S. Patent 5,521,070), Ritter et al. (1991. Journal of Biological Chemistry. 266:1043-1047) and Ciotti et al. (1996. Biochemistry 35:10119-10124).

Builder et al. teach expression of DNA encoding a desired polypeptide. Builder et al. teach that suitable host cells appropriate for the expression of the DNA encoding the desired polypeptide include useful mammalian host cells lines such as mouse sertoli cells (TM4) (column 14, lines 3-65). Builder et al. also teach that polypeptides of interest include molecules such as factor VIIIC and factor IX, among many others (see column 8, lines 24-65, especially lines 45-46, and column 9, lines1-9). Builder et al. do not present working examples of Sertoli cells comprising vectors encoding these factors, although they suggest such cells and vectors. Builder et al. also do not specifically mention B-UGT.

Meulien et al. teach that in the sequence coding for Factor IX, there is a signal sequence encoded in the cDNA (see column 1, lines 62-67). Meulien et al. do not teach Sertoli cells.

Ritter et al. teach the cloning of cDNAs for two bilirubin UDP-glucuronosyltransferases (B-UGT in the instant claims). These have signal peptides (see abstract). Ritter et al. also teaches diseases resulting from loss of bilirubin glucuronidating activity, such as Crigler-Naijar syndrome (see page 1043, right column). Ritter et al. do not teach Sertoli cells.

Ciotti et al. also teach vectors comprising bilirubin UDPglucuronosyltransferase and mutants thereof, and the study of the activity of the proteins expressed from the vectors in COS cells. See abstract, page 10120, and the Discussion section. Ciotti et al. do not teach Sertoli cells.

At the time of the invention of the instant application, one of ordinary skill in the art would have been motivated to express in cells any biological factor (polypeptide) of interest, especially polypeptides of importance to human biology, such as Factor VIII, Factor IX, or bilirubin UDP glucuronosyltransferase, as taught by Gorman, Builder et al., Meulin, and Ritter et al., so that the polypeptide could be produced and either used for therapeutic purposes or studied in vitro, for example to gain a better understanding of how mutations affect function. It would have been obvious to the ordinary artisan to use any cells known in the art to be useful for expressing polypeptides. The ordinary artisan would have been aware of teachings of expression of polypeptides in different types of cells, as such references would all be analogous art and different cells that were shown to be successful for expression of biological factors (polypeptides) would be art-recognized equivalents of one another. The particularly good production of biological factors in Sertoli cells, taught in the working examples of Gorman, as well as the claims of Gorman which suggest producing any biological factor in sertoli cells, would motivate the ordinary artisan to produce biological factors of interest in Sertoli cells. Further, Builder et al. specifically lists sertoli cells as among useful mammalian cells and Factor IX as among polypeptides of interest. One would have been motivated to use a promoter that functioned in the cells, as well as 3' termination signals, so that the polypeptides would be expressed. Since many biological factors, such as Factor VIII, Factor IX, and B-UGT, have signal sequences, which are upstream of the coding region of the rest of the protein and downstream of any promoter, there would have been motivation to include those signal sequences (encoding signal peptides) in vectors for expressing the biological factors. Success would have been expected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa J. Gansheroff whose telephone number is (703) 605-1203. The examiner can normally be reached 9 AM - 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached at (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242 for regular communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Dianiece Jacobs whose telephone number is (703) 305-3388 or to the receptionist whose telephone number is (703) 308-0196.

LG
March 20, 2001

JAMES KETTER
PRIMARY EXAMINER